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Tuberculosis Chemotherapy with Hydrazine Derivatives of Isonicotinic Acid

Ninety-two patients with moderately or far-advanced pulmonary tuberculosis, classified largely as progressive and caseous-pneumonic, have been treated with the hydrazide of isonicotinic acid (Rimifon) and its isopropyl derivative (Marsilid). All patients had positive sputum and active disease before institution of therapy. Forty-five were toxic and febrile.

Patients, divided into groups, were treated with 2, 4, and 10 mg. per Kg. of Marsilid and 4 mg. of Rimifon for from 4 to 15 weeks.

Complete elimination of fever and toxicity occurred within 2 to 3 weeks in all cases. Appetite increase and restored sense of well-being were matched and overshadowed by weight gains which varied up to 64 pounds and averaged 18 pounds at an average of 9 weeks of treatment. Sputum negativity was obtained in 25 % of patients in from 4 to 15 weeks of treatment and in another 28 %, sharp reductions from consistent plain smear positivity to "occasionally positive" occurred. Cough and expectoration were completely eliminated, or almost so, in from 2 to 3 weeks.

Among the 92 cases, in from 4 to 15 weeks, cavity closure occurred in 2 cases, marked reduction in cavity size was noted in 33 cases, clearing of exudate occurred 17 times. Marked simultaneous diminution in several cavities within the same lung was seen 3 times. Extension of exudate occurred 4 times and was minimal. One equivocal new cavity appeared at the site of a pre-therapy exudate.

There was no death due to progression of tuberculosis or to therapy.

Cure or marked improvement has been seen in cases of tuberculous laryngitis, tuberculous otitis and tuberculous glossitis.

Toxic effects of Marsilid and Rimifon therapy include hyperreflexia, leg-twitching, constipation, vertigo and reflex disturbance of micturition. However, every patient has been benefited by therapy.

Clinical investigation of these previously untried new compounds, the hydrazide of isonicotinic acid (Rimifon) and its isopropyl derivative (Marsilid) reveals that they are potent agents for the treatment of human tuberculosis. (Dis. Chest, April 1952, I. J. Selikoff & E. H. Robitzek)

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The Therapeutic Use of Oxygen in Industrial Medicine

It has been generally accepted that provision for the administration of oxygen is a requirement for the well-equipped industrial first aid station or industrial medical department. Unfortunately, this equipment has been maintained and utilized principally for the treatment of cases of acute asphyxia and as a treatment of last resort for a variety of terminal conditions. Experience has shown that there is a much wider application for this valuable gas than is often appreciated. It can be used to advantage for many industrial exposures, not only as a therapeutic agent but also as a prophylactic measure to prevent complications resulting from such exposures.

Exposure to noxious gases or fumes may result in damage to lung tissue so that it is incapable of handling the exchange of oxygen from the atmosphere to the blood stream. These gases or fumes may provide an atmosphere deficient in oxygen, or they may combine directly with the blood or tissue to the exclusion of oxygen. It is of interest to note that in cases of exposure to many noxious gases or fumes the changes found in the lungs following an undue exposure are not unlike the changes noted in the lungs of persons with various respiratory and cardiac diseases of non-occupational origin. For these respiratory and cardiac diseases, oxygen is widely used in treatment, since they are associated with the inability of the lungs to diffuse oxygen into the blood stream, or the inability of the blood to carry an adequate amount of oxygen to vital tissues. In both the occupational and non-occupational conditions there is a lack of oxygen, or anoxia, and, to combat this anoxia, oxygen is of proved value. It has also been demonstrated that oxygen administered promptly after exposure to certain irritant gases relieves the symptoms promptly and prevents complications due to the exposure.

In almost any given industrial plant an appraisal of the materials handled and processes involved should present a picture as to what sort of exposure to noxious gases or fumes might be anticipated. Accidental spillage of certain acids for example, can result in serious exposures, yet under normal methods of handling there would be no hazard. A quantity of nitric acid spilled on wood or some sawdust in a confined space can result in the evolution of oxide of nitrogen fumes in quantities sufficient to cause severe injury.

There is available a detailed classification of noxious gases in the monograph, "Noxious Gases," by Henderson and Haggard, published in 1943. The following excerpts give a classification of irritants, asphyxiants, and anesthetics, based on morbid physiological response to them.

"I. Irritants:

A. Those affecting mainly the upper respiratory tract. Examples: Ammonia, hydrochloric acid, sulphuric acid, hydrofluoric acid and acetic anhydride.

B. Those affecting the upper respiratory tract and also deeper structures, such as the bronchi. Examples: Chlorine, sulphur dioxide, bromine and iodine.

C. Those acting primarily upon the lungs and to a less extent upon the upper respiratory tract. Examples: Ozone, nitrogen dioxide (nitrous fumes), phosgene.

D. Organic vapors which do not follow the general rule as to solubility in relation to location of action. Examples: Acrolein (acrylic aldehyde), dimethyl sulphate, halogenated organic compounds.

II. Asphyxiants:

A. Simple. These act primarily because when exposure to these gases occurs there is either insufficient or no oxygen present. Examples: Nitrogen, hydrogen, helium, methane, ethane, propane and acetylene.

B. Chemical Asphyxiants. These are probably the most important of all because they are responsible for more deaths than any other class of noxious gases. Examples: Carbon monoxide, cyanides and cyanogen compounds. Carbon monoxide is an asphyxiant because it has a property of combining with the hemoglobin of the blood and excluding the oxygen from the hemoglobin. Cyanide is an

asphyxiant because it acts upon the tissues and temporarily deprives them of the capacity to use oxygen which the blood brings.

III. Volatile Drugs and Drug-Like Substances: The one physiological action common to these substances is that of inducing symptoms of anesthesia when inhaled in a sufficient quantity. Examples: Ethers, gasoline, cholorinated hydrocarbons, methyl alcohol, and many others."

Certain metal fumes are capable of producing lung irritation, and cadmium, of all the various metal-fume exposures, seems to stand out as being capable of producing delayed lung changes. The lungs seem to bear the brunt of the assault from the inhalation of the fumes. There is little irritation of the upper respiratory system, and usually the first symptom noted is a dryness of the throat and a feeling of soreness in the chest. This is followed by cough, with headache and dizziness. After 12 to 36 hours there occurs severe constricting pain in the chest, and marked dyspnea. This delay is comparable to that seen in phosgene and nitrogen dioxide poisoning. Death may occur from undue exposure to cadmium fumes. While reports are not available upon the use of oxygen exhaled against pressure in such cases shortly after an exposure to cadmium fumes, from the symptomatology and clinical findings, oxygen therapy would be expected to be a treatment of choice for such exposures.

While time is important in cases of exposure to irritants, cases of exposure to asphyxiants, of course, require oxygen more promptly. In cases exposed to asphyxiants, positive pressure breathing is not necessarily required. In such cases in which breathing has stopped, artificial resuscitation should be started at once, and oxygen should be administered while the artificial respiration is in progress.

It is frequently impossible to ascertain the degree of exposure to a noxious gas or fume. For this reason it is safe to assume that if an exposure exists, the victim should be given the benefit of the doubt and should receive oxygen.

In the industrial plant there are many other conditions that can occur to employees besides exposures to noxious gases and fumes that are indications for oxygen therapy. To mention a few, it is an established form of emergency treatment for acute heart attacks, such as coronary occlusion. Severe traumatic conditions presenting evidence of shock, such as fractures, head injuries and severe burns, are indications for the prompt administration of oxygen. It has also been of proved value in electrical shock as well as heat stroke.

The widespread use of oxygen in hospitals, institutions, by rescue teams, and even in the home, is adequate proof as to the safety in its use when reasonable precautions are taken. It is essential, however, that oxygen should be administered by an attendant who understands the operation of the oxygen equipment. Oxygen should be given in an industrial medical department only by a physician, or by a nurse, or a qualified first aid attendant who is trained in its administration and is working under the supervision of a physician. (Indust. Med. & Surg., April 1952, T. W. Nale)

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The Nonvisualized Gall Bladder

The authors of this paper believe that confusion still exists concerning the proper interpretation of at least one finding - the nonvisualized gall bladder. This confusion may date back to the early days of cholecystography, when sufficient experience had not yet been acquired to standardize the administration of the dye, the technic of the filming or the interpretation of the various x-ray appearances. More recent reports indicate a high incidence of calculi (approximately 90 %)when the nonvisualized gall bladder is removed. At an earlier date, however, some doubt was cast on the pathologic status of the gall bladder that was not visualized after administration of the dye.

The authors reviewed 232 cases, of which 226 patients had cholecystograms and 6 had other studies; all had undergone gallbladder surgery.

This review, combined with a study of the physiology and the reports of other authors, indicates that because of nonvisualization under certain circumstances gall bladders may be erroneously reported as diseased:

(1) When the gall bladder has already been removed, unknown to the patient.

(2) When the dye was not ingested (many patients do not understand the instructions) or the fasting requirements were not properly observed.

(3) When the dye was not properly absorbed from the small bowel because of:

(a) pyloric obstruction or intestinal obstruction;

(b) active duodenal ulcer and hyperchlorhydria;

(c) too rapid passage of the dye through the small intestine in severe gastrointestinal upsets or through the improper use of laxatives;

(d) disease of the small bowel;

(e) pancreatic obstruction (possibly).

(4) When the dye cannot reach the gall bladder because of:

(a) severe liver disease, such as cirrhosis;

(b) obstruction of the hepatic or cystic ducts (stones or tumors).

(5) When there is physiologic stasis. Brewer has shown that if a patient has been limited to a fat-free diet or has been unable to retain any food, the gall bladder may not have emptied for several days. The bile in the gall bladder will be thick and concentrated. When cholecystography is attempted in the presence of such physiologic stasis, fresh dye-laden bile is unable to enter the gall bladder; hence, it does not visualize even though disease may not be present. In other cases, partial concentration of the dye results in faint shadow. Similarly, morphine and other narcotic drugs may adversely effect the filling of the gall bladder with the dye-laden bile.

(6) When there is a cholecystic anomaly (such as situs inversus, absence of the gall bladder and so forth) or displacement of the gall bladder.

To obviate nonvisualization in gall bladders that are not diseased, the following procedures are suggested: Careful instructions to the patients and an inquiry into all nonvisualization cases to be certain that the instructions were carefully followed. Repeat cholecystography studies in all cases of non-

visualization. Sometimes the repeat examination should be delayed for a considerable time. (For instance, if the patient has been experiencing rather severe gastrointestinal symptoms, the repeat study should be put off until a quiescent period has been attained.) When possible, gall-bladder studies should not be attempted on patients who are acutely ill; if attempted, great care should be exercised in evaluating nonvisualization in such cases. Since drugs such as morphine and other narcotics, adrenalin, pituitrin, acetylcholine, eserine, histamine, Banthine and nitrates may possibly influence the physiology of the biliary tract, a careful check of the medication the patient is receiving is advisable. Patients on fat-free diets should probably be allowed to ingest some fat about 6 hours before taking the dye to ensure an empty gall bladder that can receive the dye. It is frequently necessary to check the rest of the gastrointestinal tract by means of gastrointestinal series, barium enema and occasional liver-function tests, as stressed by Tracey. (New England J. Med., 27 March 1952, F. Martin & A. G. Massimiano)

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The Effectiveness of Various Drugs for the Prophylaxis of Seasickness

Although certain antihistaminic drugs exert considerable protection, prophylaxis against motion sickness does not depend upon the antihistaminic action of the drug. Thus pyranisamine (neoantergen) maleate and phenindamine (thephorin) tartrate are ineffective in doses eliciting strong antihistaminic action. The effectiveness of dimenhydrinate (dramamine), diphenhydramine (benadryl) hydrochloride and chlorcyclizine (perazil) hydrochloride must therefore be attributed to other pharmacologic properties. Their anticholinergic action seems the most plausible, since other drugs with central atropine-like action, such as scopolamine hydrobromide and trihexyphenidyl (artane) possess similar prophylactic properties.

This report is of the continuation of tests on drugs of possible value through a cooperative study by the Army, Navy and Air Force. Subjects were drawn from all 3 services; the transports were supplied by the Military Sea Transport Service, United States Navy, while the supervisory and assisting personnel were from both the Navy and Air Force. The preparations tested were selected for a variety of reasons. Diphenhydramine was chosen as a control drug because of its known value as a protective. A mixture of diphenhydramine and scopolamine has been the most effective remedy against airsickness, but had not been given a trial against seasickness. Similarly, scopolamine aminoxide hydrobromide (scopodex) and the scopolamine aminoxide-diphenhydramine mixture give significant protection against airsickness, but had not been tested at sea. Preliminary studies by MacKay with the antihistaminic prophenpyramine (trimeton) maleate against airsickness were promising. A long-acting antihistaminic, N (α methyl β dimethyl aminoethyl) phenothiazine hydrochloride (lergigan) has been reported to protect against seasickness. Furthermore, it is known to prevent the compulsive turning of animals after intracarotid injection of diisopropyl fluorophosphate (DFP), a

property possessed by certain other effective anti-motion sickness drugs. N-benzhydryl N methyl piperazine dihydrochloride (preparation 47-83) was chosen because of its close chemical similarity with chlorocyclizine (perazil), which has been shown to afford significant protection against both air and seasickness. Methaphenilene (diatrin) hydrochloride, another antihistamine, and β diethylamino ethyl-2-thienyl (α-2-cyclopentenyl) acetate hydrochloride (preparation W-290), an antispasmodic, have each been reported to give some protection against the emesis following apomorphine injection. The strong anticholinergic properties of 1,1-diphenyl-N,N-dimethyl 4-piperylidene methane methyl sulfate (prantal) suggested that it be included.

Of the various preparations demonstrated to have significant protection against seasickness in the present as well as a previous study, lergigan appears to be the most promising, not only because of an apparently greater protection but also because of its long duration of action. This latter property would be especially valuable in long sea voyages during which frequent medication may be harmful as well as inconvenient. Additional studies are urgently needed to confirm and extend these observations.

Lergigan, trimeton, benadryl, scopolamine hydrobromide mixture and preparation No. 47-83 all provided approximately equal protection against seasickness. No preparation was significantly superior to that of benadryl although the observed per cent protection afforded by lergigan was slightly greater.

No protection was given by the antihistaminic methaphenilene (diatrin), or by the antispasmodic W-290 or prantal. Slight protection, not significant at the 1 % level, was obtained with scopodex alone or with a mixture of benadryl and scopolamine aminoxide.

Side effects were minimal in all cases except among those persons receiving the scopolamine aminoxide. When 2.0 mg. doses of the latter were given 3 times daily, hallucinations, nightmares, dry mouth, blurred vision and ringing in the ears were observed. When 1.0 mg. was given combined with 25 mg. of diphenhydramine, there were no hallucinations but the incidence of nightmares, dry mouth and blurred vision was still increased.

There was an inverse relation between the incidence of vomiting and the age of the subject. No relation could be detected between the number sick and the compartments in which they were quartered nor with the degree and/or duration of motion therein under the conditions of these sea trials. (Am. J. Med., April 1952, Maj. H. I. Chinn (MSC), USAF, LCDR S. W. Handford (MSC), USN, CDR T. E. Cone, Jr. (MC) USN, & LTCOL P. K. Smith, USAF)

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Recommended Treatment for Potential Rabies

Specific recommendations for the management of persons who have been exposed to a rabid or potentially rabid animal are found in the Report of the First Session of the Expert Committee on Rabies, World Health Organization, Technical Report Series Number 28, dated November 1950. The entire report may be

purchased from the World Health Organization at the price of 20 cents.

Four paragraphs from the Report, containing the most practical specific advice are quoted:

"Hyperimmune Antirabies Serum. For many years the possible prophylactic use of rabies-immune serum has been recognized, and numerous experiments have pointed to its practical potentialities. More recent experimental work employing quantitative procedures has definitely shown the superiority of hyperimmune serum, especially when combined with a course of vaccine, over the use of vaccine alone after exposure to peripherally introduced street virus. Practical means of producing this serum in large animals such as sheep and the concentration of the specific antibody are available. The use of highly potent hyperimmune serum preceding a course of vaccine gives promise of saving most of those cases of human rabies in which a short incubation time does not allow a sufficiently long period for the development of active immunity. In view of these experimental findings, the committee feels that at the present time serum combined with vaccine offers the best promise as a means of preventing rabies after severe exposure and strongly recommends the setting-up of a field trial in human beings thus exposed.

"Biological Test for Confirmatory Diagnosis of Rabies. The confirmatory intracerebral inoculation of mice or hamsters for the presence of street virus in instances of questionable diagnosis on pathological grounds is definitely recommended. The mouse is the animal of choice, but where not easily available, hamsters may be substituted because of their high susceptibility to street virus infection.

"Local Treatment of Animal-Bite Wounds. The committee recommends the immediate treatment of bite wounds inflicted by rabid animals, or animals suspected of being rabid, by thorough cleansing with soap or detergent solution. Such treatment does not preclude the subsequent application of agents for the suppression of bacterial contamination, such as antibiotics.

Later, as information is obtained on the protective value of antirabies hyperimmune serum, consideration should be given to its use for local treatment by infiltration of the tissue about the site of exposure.

"Indications for Vaccine Treatment. The committee considered the variation in indications for vaccine treatment at present used throughout the world. There was general agreement along the lines set forth in table I, which has been formulated with a view to reducing to a minimum the number of persons subjected to treatment unnecessarily.

"Fairly often a situation arises in which a person previously exposed to infection and treated with vaccine is re-exposed to infection with rabies. The question as to whether treatment should be re-instituted and, if so, on what basis, must be answered. It is recommended that, if this situation arises within 3 months of the first course of vaccine, no further treatment is necessary unless the second exposure is of a severe type. If the interval is between 3 and 6 months, 2 reinforcing doses of vaccine, 1 week apart, are indicated, whereas if more than a 6-months' interval has elapsed the treatment should be on the same basis as if it were an original exposure.

TABLE I. INDICATIONS FOR VACCINE TREATMENT

Nature of exposure	Condition of biting animal		Decision as to vaccine treatment at time of possible exposure
	At time of exposure	During observation period of 10 days	
I. No lesions; indirect contact only	healthy or rabid	healthy or rabid	none
II. Licks:			
(1) unabraded skin	healthy or rabid	healthy or rabid	none
(2) abraded skin or mucosa	(a) healthy	healthy	none
	(b) healthy	clinically suspicious or proven rabid	start treatment at appearance of first suspicious signs
	(c) suspicious	healthy	start treatment immediately; stop treatment if animal remains normal for 3 days
	(d) animal rabid, escaped, killed, or unknown		start treatment immediately
III. Bites	(a) healthy	healthy	no treatment, except if bites are multiple, or face, head or neck bites; then treat as in III (c)
	(b) healthy	clinically suspicious or proven rabid	start treatment at appearance of first suspicious signs
	(c) suspicious	healthy	start treatment immediately; stop treatment if animal remains normal for 3 days
	(d) animal rabid, escaped, killed, or unknown; or any bites by jackal, wolf, fox, or other wild animal		start treatment immediately

Note: Bites on the head, neck, and shoulders, deep multiple wounds, and those inflicted by wild animals involve a greater degree of risk, and patients should be treated accordingly.

"Occasionally, marked allergy to rabies vaccine manifested by angioneurotic edema, fever, adenopathy, shock, etc., is encountered. This may be during the course of immunization or, more often, following the administration of the first dose to a person who has previously received rabies vaccine. It is suggested that this difficulty may be circumvented by a change to vaccine made from the brain tissue of another species of animal (i.e., from rabbit-brain vaccine to sheep-brain vaccine)." (Preventive Med. Div., BuMed)

Note: Complications of vaccine administration, and their relief, are described in the Medical News Letter, Vol. 18, No. 3, pp. 2-3, 10 August 1951. Further advice concerning "Second Courses of Rabies Vaccine" is given in the News Letter for 11 January 1952, Vol. 19, No. 1

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Periarteritis Nodosa

Periarteritis nodosa (polyarteritis or panarteritis) is a disseminated disease characterized by focal inflammatory lesions of the arterioles of unknown origin which has a serious prognosis. In 1944 Boyd made a clinical review of 395 cases reported in the literature, and to the present time more than 400 cases have been reported.

Although the etiology of periarteritis nodosa is unknown, several interesting speculations have been made. Some years ago it was suggested that this

disease might result from the effects of high blood pressure on a congenitally defective vascular system or that it might be an unusual manifestation of syphilis. The belief has been advanced that streptococcic or virus infections might play a role in its etiology. Since a history of rheumatic fever is found in about 10 % of cases and at autopsy findings suggestive of rheumatic pancarditis are not uncommon, this possible interrelationship has been stressed. Additionally, the similarity of periarteritis nodosa and malignant nephrosclerosis has been described by Fahr.

In recent years the hypothesis that periarteritis nodosa is the result of an allergic vascular reaction has been suggested. In about 20 % of cases there is a history of allergic manifestations as asthma, skin rashes, eosinophilia and diarrhea. As the onset of the disease frequently is preceded by an infection, the allergen in most cases is presumed to be of a bacterial nature, but cases have been reported following serum sickness and reactions to sulfonamides, iodine, thiourea and other substances. Rich and his coworkers demonstrated that ACTH and cortisone were able to inhibit the experimental cardiovascular lesions produced by anaphylactic hypersensitivity in a high percentage of experimental animals.

Present opinion is that multiple etiologic factors may be involved in the production of this disease with an allergic reaction to either drugs or infectious processes playing a prominent role. There is much clinical and histologic evidence to suggest that periarteritis nodosa may be related to such diseases as disseminated lupus erythematosus, rheumatic fever and rheumatoid arthritis, Henoch and Schoenlein's purpura, scleroderma and dermatomyositis. They may possibly be merely the different clinical manifestations of various agents with the same underlying pathophysiologic process. In this respect, it is interesting that Selye has been able to produce in rats the lesions of nephrosclerosis, rheumatic carditis, rheumatoid arthritis and periarteritis nodosa by the repeated administrations of desoxycorticosterone or desoxocortisone (Reichstein's "Compound S"), two mineralocorticoids from the adrenal cortex. Additionally, administration of lyophilized anterior pituitary tissue, renal pressor substance and different forms of stress have experimentally produced periarteritis nodosa.

These and other observations led Selye to hypothesize that "as a result of exposure to stress (e.g., that caused by emotional stimuli, infections or intoxications), the adrenal may under certain circumstances respond with a disproportionate overproduction of either the gluco- or the mineralocorticoids," and that periarteritis nodosa, a disease of maladaptation, "could perhaps be the result of an unbalanced excess of the latter type of steroid". More recently two glucocorticosteroids, Kendall's "Compounds E (cortisone) and F," have shown temporary inhibiting effects against rheumatoid arthritis, rheumatic fever, disseminated lupus erythematosus and periarteritis nodosa, the same diseases which, according to Selye, can be produced in rats by administering the mineralocorticoids, desoxycorticosterone and desoxocortisone. The pituitary adrenal corticotrophic hormone (ACTH) has had an effect in these diseases practically identical to cortisone, this effect depending on increased adrenal output of glucocorticoids under ACTH stimulation.

As this disease may possibly be the result of an abnormal immune response, it is recommended that a careful search be made for possible allergens. Sulfonamide drugs especially are contraindicated, even in the treatment of coincidental or secondary infections, should they occur in the course of periarteritis nodosa since they may in certain instances play a role in the etiology of the disease. During the period that ACTH and cortisone have been available for clinical use, reports have been made on the treatment of about 14 cases. These reports are encouraging but the remissions obtained seem only temporary. The effect of these hormones is probably suppressive rather than curative.

Shick and his coworkers treated 2 cases of periarteritis nodosa with ACTH and 3 with cortisone. All showed initial improvement but at the time of the report, 2 who had received cortisone (for 75 and 146 days or 3.6 and 13.4 Gm. of cortisone respectively), died. On a clinical basis, these deaths resulted from cardiorenal failure; postmortem examination revealed widespread visceral infarctions secondary to obliterative fibrosis of the blood vessels (the healing stage of Arkin). In a single case treated with ACTH by Carey, serial muscle biopsies showed healing changes. Irons and others reported remission 5 days after the institution of ACTH treatment in 1 patient (who later developed asymptomatic occlusion of the left dorsalis pedis artery). Clinical and pathologic remission with physical improvement lasting up to 14 months has recently been reported in 1 patient receiving prolonged ACTH therapy.

These and other reports suggest that ACTH or cortisone should be given as early as possible in the course of this disease. Though it is not established definitely, the possibility that ACTH or cortisone administered to the patient with extensive disease might result in an increase in symptomatology or hasten death by widespread vascular occlusion secondary to healing must be considered. (J. Missouri M. A., April 1952, Finn Ficher & C. S. Gillmor)

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A New Approach to the Problem of Postoperative Pain

Efocaine is described as producing a local anesthesia lasting for more than a week and consists of procaine and butyl amino benzoate in a non-toxic vehicle composed essentially of propylene glycol and water. The rationale for the mechanism of this prolonged duration is new and challenging.

The problem of postoperative pain control is concerned with 2 basic factors: (1) the pain arising directly from the surgical procedure which is local in origin and (2) the referred or reflex pain which is of visceral origin. It is a common observation in abdominal symptomatology that the hollow intraperitoneal viscera, which are medially situated in regard to their embryonic development, may produce two different types of pain, namely, true visceral pain and referred or reflex pain. The viscera themselves are insensitive to the stimuli that ordinarily provoke pain on the body surfaces, for example, burning and cutting. However, it is agreed that pain is appreciated by a visceral organ when it is exposed to factors which inhibit or alter its function. Such visceral pain has characteristic and well

defined features. They are typically, if not always, medial in location, e.g., the epigastrium area in the case of the stomach; above and around the umbilicus in the case of the small intestines and the appendix; and below the umbilicus in the case of the colon. Such true visceral pain is usually only imperfectly localized by the patient and is unassociated with hyperalgesia of the corresponding area. A common example of such medial visceral pain in a lateral organ is the initial umbilical pain occurring in appendicitis.

Referred or reflex pain is felt on a body surface at a site which generally is determined by the location of the organ, although it may be projected on to a distant area of the abdominal wall or other somatic surface. These referred pains are associated with hyperalgesia and muscular rigidity and, therefore, are well defined.

True visceral pain arises from the focus and is conducted through the splanchnic nerves. Its site is determined by the spinal segment corresponding to the embryologic development of the organ. The mechanism of referred pain is different and has been the subject of much controversy.

Efocaine, a prolonged aqueous local anesthetic, was clinically evaluated for the control of postoperative pain in a series of 100 surgical cases. An excellent control of postoperative pain was achieved, even in instances in which much visceral manipulation occurred. The postoperative drug requirements were virtually eliminated for the treated patients.

There were no local or systemic reactions nor were there any complications observed in the treated patients. The convalescence of the patients was much more pleasant and early ambulation facilitated. Less nursing care was required.

It is concluded that efocaine is a safe and effective local anesthetic that is indicated in the control of postoperative pain. (Am. J. Surg., April 1952, A. H. Iason & H. E. Shaftel)

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Use of Intra-Arterial Nitrogen Mustard Therapy in the Treatment of Cervical and Vaginal Cancer

Sixteen patients with carcinoma of the cervix and/or vagina were treated by fractionated intra-arterial HN_2 therapy administered through the lower abdominal aortic route.

Clinical effects included relief of pain and dysuria and an increase of appetite and well-being. Side effects and complications observed were mild nausea, bleeding from cannula site following discontinuance of therapy, hemorrhage and extravasation of mustard into soft tissue.

Effects on the lesion included regression of the local disease in 8 patients, reduction in the palpable size and consistency of the pelvic mass in 4 and ulceration and necrosis of the vagina in 4 patients. Two patients in the series failed to show a satisfactory response.

The results suggest the use of the method either alone or in combination with radiation therapy in palliative treatment of cervix cancer; and possibly as an adjunct to radiation therapy in definitive treatment. (Am. J. Obst. & Gynec., March 1952, J. K. Cromer, J. C. Bateman, G. N. Berry, J. M. Kennelly, C. T. Klopp & L. I. Platt)

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Toxic Psychosis Following Nitrogen Mustard Therapy

The case is presented of a 25 year old white male veteran with Hodgkin's disease who developed a toxic psychosis lasting 3 weeks after a single course of nitrogen mustard (HN_2) therapy. Evidence is presented implicating this drug as the etiologic agent in the production of the psychosis. This appears to be the first time such a complication has been reported.

In the consideration of this toxic psychosis, a reversible process of unknown nature produced by the action of HN_2 on the nervous system must be surmised. This toxic effect apparently has not yet been reported by other investigators. However, Burchenal employed SK-137, another nitrogen mustard derivative and observed 2 cases with transient toxic psychosis lasting from 12 to 24 hours, necessitating the discontinuance of the use of this compound. He also noted that some patients complained of nervousness and bad dreams after the use of SK-136, another mustard derivative, whose toxicity is of the same level as HN_2.

Inasmuch as the blood picture in the authors' patient did not reveal a severe anemia during a period of psychosis, this possible etiologic factor may be eliminated. It is also difficult to impute importance to the degradation products of the degenerating lymphoid tumors because the psychotic reaction was not observed during the second and third courses of mustard therapy.

In the consideration of Hodgkin's disease per se, as responsible for the psychosis, a review of the older literature failed to reveal any specific mention of abnormal mental trends in the presence of Hodgkin's disease.

The occurrence of a psychotic episode after the first course of the HN_2 compound and not after the second and third series of injections cannot be explained readily except to rationalize that a tolerance may have developed. A more satisfactory cause and effect explanation awaits further elucidation of the biologic action of these toxic substances.

From their survey the authors draw the general conclusion that mental symptoms are exceedingly rare in Hodgkin's disease with or without intracranial involvement. When present, these mental symptoms are generally found with localizing neurologic signs. The latter were entirely absent in their patient.

The authors are therefore convinced that their patient's psychotic episode was directly due to the influence of the nitrogen mustard compound with which he was treated. (J. Nerv. & Ment. Dis., April 1952, B. Roswit & J. E. Pisetsky)

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Primary Malignant Tumors of Nerve

Eight cases of tumor involving anatomically named nerves, which were in the files of the Armed Forces Institute of Pathology, have been subjected to detailed study. This work was undertaken to establish the histological characteristics of tumors originating in nerves in order to facilitate the study of a large group of soft-tissue tumors that perhaps might be recognized as neurogenous. Records, descriptions and slides from these 8 cases were available, and multiple sections of each tumor were cut and examined, using the following stains: hematoxylin and eosin, Masson's trichrome, periodic acid (Schiff), Wilder and Bodian.

In these 8 primary malignant tumors of nerve, the tumor cell was most frequently elongated and spindle-shaped; in myxomatous focuses, it was found to have anastomoses with its neighbors. A distinct tendency to grow in groups was manifested by palisades and fasciculi, often separated by thin-walled vascular channels. Sclerosis of these vessels in 1 instance resulted in a peculiar radiating or pin-wheel arrangement of the tumor cells. Except in 1 highly undifferentiated tumor, the cytoplasm was moderately abundant, palely eosinophilic, and variablyhomogeneous,granular or irregularly vacuolated. Shortening of the tumor cells in 5 instances produced an epithelial-appearing pattern. In 3 of these 5, the arrangement of cells in alveolar groups or columns and the presence of numbers of multinucleated forms strongly suggested melanoma. Reticulin was arranged in a sleevelike fashion about the spindle-shaped tumor cells but merely surrounded and outlined groups of the epithelial or melanoma-like cells. Despite the considerable variation in pattern, all the tumors were regarded as histogenetically related. Basically they appeared to be the result of neoplastic transformation of Schwann cells. (Cancer, March 1952, Ira Gore)

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Krilium

The new soil conditioner Krilium has received a great deal of publicity since a preliminary announcement was made at the Philadelphia meeting of the AAAS last December. It is a soil conditioner and not a fertilizer. No claims are made for fertilizer value of the material, but the improvement of physical conditions resulting from its use may cause the plant nutrients of soils, as well as those of fertilizers, to become more useful to growing plants.

Krilium is a pale-yellow powder that can transform tight, gummy clays into friable materials of crumblike structure. Even though it must dissolve in the soil moisture to promote physical improvement, Krilium does not move or leach below the zone of application; hence its effectiveness in the plow-depth may be somewhat limited by impervious subsoil conditions.

Chemically this material is a sodium salt of a hydrolyzed polyacrylonitrile. It is a long-chain, organic molecule, somewhat similar in structure to the nylon molecule and it is nontoxic at the rates of application used. It improves soil structure by aggregating and loosely cementing clay particles together in much

the same way that decomposing organic matter acts. Yet the new compound decomposes in the soil very slowly, at a rate not yet determined.

Krilium is one of a family of chemicals developed by the Monsanto Chemical Company at Dayton, Ohio. It is not yet available commercially but is expected to be on the market some time in 1953. The Department of Agriculture and several state agricultural experiment stations have been interested in the agricultural possibilities of this material since it was first brought to their attention. During the 1951 growing season, preliminary experiments were conducted by the USDA on saline and alkali soils in California, to find out if Krilium or closely related compounds might aid in their reclamation or in the production of more nearly normal crop yields. Favorable results were obtained, with remarkable increases in germination and stands of corn. In one case, yield increase was as much as fivefold. Other experiments at USDA field stations in Alabama, Tennessee, Pennsylvania and Wisconsin are not yet fully evaluated, but the material has been shown to produce definite improvement in the physical character of heavy clay soils. Better aeration, which is necessary for normal root development, is one of the beneficial effects.

Best results are obtained when Krilium is applied to a soil previously prepared for seeding. The dry powder should be spread uniformly, and mixed immediately and thoroughly to the desired depth. Rates of application range from 400 to 2,000 pounds per acre when incorporated in soil to a 6-inch depth. Unfortunately, the possibilities of widespread agricultural use do not seem large at present in view of proposed high introductory prices.

There are, however, a number of specialized agricultural uses for which the material should be practical - for example, preparation of potting soils, greenhouse production of flowers and vegetables, home flower and vegetable gardens located on heavy soil and possibly certain market garden areas where high-value specialty crops are grown. For garden plots Krilium should be mixed thoroughly to spade depth, using a rate of about 0.1 %, or 1 lb. to 20 square feet. In the case of potting soil, 1 oz. should suffice for 100-150 lb. of soil. Another field of utilization includes the stabilization of soil in road cuts and similar engineering projects, where an application of 1 lb. per 100 square feet applied on the surface serves to hold the soil while turf is being established from seed. Additional research is planned by the Bureau of Plant Industry and by state agricultural experiment stations. One of the items receiving attention in the Bureau is the treatment of a narrow band of soil above or around the seed or a shallow overall treatment for the purpose of improving emergence. (Science, 11 April 1952, R. Q. Parks, USDA)

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Recent Clinical Experience with the Grid in the X-Ray Treatment of Advanced Cancer

A preliminary report is presented on the use of roentgen therapy with a grid and high dosage in patients with advanced, hopeless cancers. Physical measurements indicate that there is an advantage in depth dose with the grid over the conventional open portal method. This is predicated on the assumption that normal tissues can tolerate the larger doses mentioned in this report. One hundred and twenty-seven patients have completed treatment during a 15 month period. The primary aim of palliation and prolongation of useful life seems to have been achieved in a number of these patients. Further experience and studies regarding dosage (over-all time, fractionation, quality of radiation) and normal tissue tolerance may indicate that this is a valuable method in obtaining palliation and occasionally cure in patients with advanced cancer. The most promising results were obtained in cancer of the lung and urinary bladder. (Radiology, March 1952, W. Harris)

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Acute Effects of Intravenous Administration of a Preparation of Veratrum Viride in Patients with Severe Forms of Hypertensive Disease

The use of intravenously administered Veriloid, a standardized mixture of Veratrum alkaloids, was found helpful in the management of 25 patients with malignant and severe forms of hypertensive disease in whom excessively high blood pressure levels warranted immediate vigorous treatment and also in patients who had previously failed to respond satisfactorily to oral Veratrum therapy. It was given 36 times to the 25 patients. The drug infusion was effective in lowering the blood pressure in all patients and in relieving untoward symptoms in 8 of 12 patients with hypertensive encephalopathy (crisis). Unpleasant symptoms present in 11 additional patients without hypertensive encephalopathy were relieved in 6.

Veriloid can be given intravenously with relative safety to hypertensive patients even in the presence of severe renal, cardiac or cerebral functional impairment. The drug should be administered by infusion over a period of several minutes. An initial Veriloid infusion rate of from 0.6 to 0.68 microgm. per Kg. per minute appears to be safe and effective. The blood pressure changes should be followed carefully at 1 minute intervals during infusion and at less frequent intervals for 30 minutes afterwards in order to encompass the entire "overshoot" period (time from end of infusion to maximum hypotensive response) for most patients. The effective total dose may vary from patient to patient, and in any single patient it should be computed on the basis of the vasodepressor response obtained during infusion of the drug. In general, the tendency toward a continued drop in blood pressure after infusion is stopped should be taken into account.

Slight to moderate heart-rate slowing, a desirable effect in some patients, was noted. True bradycardia attributable solely to intravenous Veriloid

administration did not occur. In no case did heart-rate slowing necessitate terminating the infusion. A significant arrhythmia was noted in 1 of 36 trials.

Nausea or vomiting occurred in 10 patients, especially when the infusion rate was faster than that recommended, and in 7 patients with hypertensive encephalopathy. With the recommended method of administration, however, vomiting did not appear to be a sufficiently severe untoward side-effect to warrant limitation of the intravenous use of Veriloid. Vomiting occurred in 5 of the patients who appeared to benefit most from the Veriloid therapy.

In spite of encouraging symptomatic responses to Veriloid infusions, the survival data for the patients studied do not indicate that the course of hypertensive disease of this severe type was materially altered by the therapy except possibly in 3 patients.

If the drug is administered slowly, with a continuous checking of blood pressure, dangerous hypotensive collapse can be avoided. The dose must be regulated, however, on the basis of the patient's weight and his vasodepressor response during infusion of the drug. (New England J. Med., 13 March 1952, N. S. Stearns & L. B. Ellis)

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Buphthalmos

The treatment of buphthalmos or juvenile glaucoma has progressed markedly in the last quarter of a century. The literature contains a number of reports of successful surgical procedures used in treating this abnormality. Several are based on the trephine operation and on goniotomy.

Associated with the trephining operation, such operative complications as loss of vitreous and subsequent phthisis bulbi have frequently been reported. It is generally agreed that the surgery of buphthalmos is much more difficult than the average glaucoma surgery. Barkan contributed notably to the technic of goniotomy.

The author's purpose in this paper is to present his conclusions that some early and late cases of buphthalmos respond to some of the older procedures, especially to cyclodiathermy used conservatively. In 5 cases here reported intraocular surgery produced little improvement in the intraocular pressure, but cyclodiathermy effected its control.

Cyclodiathermy was used in 5 of the 6 cases of this series. In 3 cases it followed cyclodialysis and in 2 was performed in conjunction with it. In 1 case, it followed unsuccessful intraocular operative procedures and 2 others, it was repeated.

In 9 of the 10 eyes the intraocular pressure was normalized. In 1 eye it was fairly normal with the use of miotics. In 1 case in which cyclodiathermy followed cyclodialysis performed at a few weeks, the visual function was retained to the extent that the child was able to go to school and the intraocular pressure was normal. In another case treatment consisted of an iris-inclusion operation in

one eye and an iris-inclusion operation combined with a corneosclerectomy in the other eye. The corneal haze cleared sufficiently to give a clear view of the grounds, and there was great improvement. Even the cloudiness disappeared in the cornea of 1 eye.

These operations are, of course, old procedures. Goniotomy would appear to be a most difficult precedure in the late type of buphthalmos with the highly opaque cornea. In these late cases, Schlemm's canal is usually closed; in all probability, therefore, an angle operation would not be of much value. It would seem that cyclodiathermy should have a place in the surgical armamentarium for this type of case. In none of the 10 eyes did global shrinkage develop, which has been feared in this type of surgery. (Am. J. Ophth., March 1952, S. B. Forbes)

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Anterior Cingulectomy in the Treatment of Mental Disease

The operation of cingulectomy - the bilateral extirpation of anterior cingular cortex - has been performed on 29 British patients with mental disease. There was 1 death due to operation. The results in the first 24 patients (16 advanced psychotics and 8 with mental illness in a basically well-preserved personality) are given after a follow up period of 18 months to 3 years.

Changes in the mental illness followed in the majority of the cases. In the psychotics, however, this was transient, and no worth-while improvement was maintained. In the others definite improvement occurred in 6 of the 8 cases. In 2 of these (a severe obsessional and an anxiety state) improvement was so great and sustained that the patients are at present regarded as cured.

A striking feature of these results has been the very slight amount of any unwanted personality change of the type seen sometimes after leucotomy. It is suggested that this operation requires further trial in certain types of mental illness marked by obsessions, tension and anxiety, in which the basic personality is well preserved. (The Lancet, 8 March 1952, C. W. M. Whitty, J. E. Duffield, P. M. Tow & Sir Hugh Cairns)

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The Membrane Filter in Water Quality Tests

The development of a rapid and accurate technic for the quantitative estimation of the bacterial content in water has long been a desideratum. This is especially true of the coliform group, which may require 4 or 5 days for completion of the usual tests. Even the plate count, which is used as a control procedure in water treatment processes and as an auxiliary water quality test, is restricted to 1 ml samples and is valid only when the bacterial density is above 25 or 30 organisms per ml. Therefore, this investigation was undertaken with the dual purpose of stimulating interest in the reduction of elapsed time and an increase in the precision of water quality examinations by means of the membrane filter technic.

The filtering apparatus is constructed of stainless steel. It consists of a funnel and receptacle. The sterile membrane is placed on a porous plate in the receptacle and the funnel is clamped over it with a bayonet locking nut. Fluid poured in the funnel passes through the membrane with the removal of the bacteria in the sample. Reduced pressure in the flask greatly increases the rate of filtration.

The filter membrane is a thin, circular disk approximately 48 mm. in diameter, composed of a cellulose derivative. The membranes are extremely porous, with tubular holes parallel to the direction of flow of the liquid. These tubes have a slightly smaller diameter at the top of the membranes. Pore size is controlled in the manufacturing process. Speed of filtration is dependent on the "Z" value of a membrane. According to Dr. Goetz, the "Z" value represents the time in seconds for 100 ml of distilled water to pass through 100 cm. of membrane at a differential pressure of 1 atmosphere. The membranes used in this investigation were "low Z".

All material and equipment used in the membrane filter technic must be sterile. Membranes, being sensitive to high temperatures (or autoclave temperature), are sterilized by exposure for 2 hours to 1 Gm. of ethylene oxide per liter of air space. After sterilization is completed, all ethylene oxide must be removed from the membrane by "flushing" with sterile air. Absorbent pads used for holding the sterile broth were washed and sterilized by boiling 5 minutes in 500 p.p.m. chlorine in distilled water, washing in boiling distilled water, and drying in a hot air oven at 90°-103° C. All other equipment is sterilized in the usual manner. The filtration equipment is wrapped in Kraft paper and is sterilized at the end of each day. It is sufficient to rinse the funnel with 30-50 ml of sterile dilution water, leaving the membrane in place. Sterilization of the funnel between filtrations is not necessary.

Application of the membrane filter technic to bacterial counts in water consists of filtration of a representative quantity of sample, choice of a suitable medium, incubation, and a count of the colonies.

The size of the water sample will depend upon the expected bacterial density. An ideal quantity will result in between 50 and 300 colonies on the membrane. This will represent a sufficiently large quantity for accurate sampling and reduce to a minimum the time and labor of colony counting. The maximum number of colonies that may be grown on a single membrane, with quantitative recovery, has not been established.

A membrane filter prepared from a cellulose derivative will quantitatively remove bacteria from water samples. Large quantities can be easily and routinely examined. Methods of cultivation are simple. Coliform determinations require approximately 18 hours in place of the present 3 or 4 days. The procedure appears applicable to the study of pathogens in water, and one specific method for Salmonella typhosa has been devised.

In general, the method promises a substantial reduction in time, material, equipment, labor, and space required for the bacteriological analysis of water and, at the same time, it indicates a likelihood that the technic will be more certain and precise in results than are the methods now in use. (Am. J. Pub. Health, April 1952, H. F. Clark & P. W. Kabler)

Nursing and the World Health Organization

A meeting of regional nurse advisers for the World Health Organization was recently held in the offices of Olive Baggallay, chief of the Nursing Section of WHO, and her associate, Lyle Creelman, in the Palais des Nations in Geneva. The problems discussed were the usual ones that supervisors face everywhere: recruitment and selection of staff, inservice education, record forms and transportation. These nurses did not have hospital wards or a local public health district; their concern was entire nations. The nursing problems vital to such countries as Cambodia, Pakistan, Israel and Paraguay were discussed with marked interest and insight.

The World Health Organization, founded in September 1948, has 78 member nations. Its headquarters are in Geneva. The field program is carried out through 6 regional offices that function in somewhat the same manner as the regional offices of the USPHS, with a health officer in charge of the various divisions and sections.

The offices of the Western Pacific region are in Manila; the regional advisory nurse is Elizabeth Hill (USA). The South East Asia offices are in New Delhi, India, and the advisory nurse is Doris Pederson (New Zealand). Eli Magnussen (Denmark) is the nurse for the Eastern Mediterranean, with offices in Alexandria, Egypt. The region of the Americas has headquarters in Washington, D. C., and the regional advisory nurse is Mrs. Agnes Chagas (Brazil). The European regional offices are in Geneva for the present, and the African region is in the process of setting up offices in Brazzaville, French Equatorial Africa.

The services of the regional staff are given to countries on an advisory basis. The staff member, whether he is the sanitary engineer, the tuberculosis control officer, the health educator, the nurse or any other of the technical group, visits a country at the request of that government and works with the health personnel in helping them solve their local problems. Some countries need help in establishing health agencies that will carry on an organized health program and others need help with an immediate problem such as the setting up of a communicable disease control program for malaria, yaws or tuberculosis.

One of the outstanding needs that the regional advisory group encounters is that for prepared personnel. Countries need different types of health personnel, depending on their culture, development and population distribution. In some countries a public health nurse would be of little value unless she was also a midwife. Other countries need workers trained as vaccinators and dressers. There is a growing recognition that nations, for the most part, should train their own personnel locally so that they will be aware of the people's needs, attitudes and interests in health and other allied matters.

Many of the countries are asking WHO for assistance in setting up schools of nursing. This raises an important question. Is the western pattern of nursing education, such as has been developed in the English-speaking countries and to which we are accustomed, the most desirable for the entire world? On a worldwide basis there is still considerable confusion regarding nursing, since both its definition and its functions vary in different societies. In many instances nursing

is only beginning to emerge as a professional service.

Some countries are asking, What are the functions of the professional nurse? Where will she fit into the overall plan? What does she need in the way of preparation to carry on her work in the community successfully? Frequently it has been found that one of her greatest responsibilities is health teaching. If the nurse really is to teach, and the people are to learn, then it is essential that she have an understanding of the language, mores and customs of the people.

In those countries where women have limited educational opportunities a nursing curriculum must be built on 5 or 6 years of general schooling, a challenge to the nurse educator.

Lack of textbooks in local languages makes curriculum planning and teaching difficult. In some schools nursing faculty spend hours translating sections of English and American textbooks so that their students will have reference material. The nursing literature of the English-speaking countries is not always adapted to the needs of nursing students with different backgrounds and customs. Very slowly, however, a body of nursing literature is being developed in those countries where nursing education is new.

In many countries the public health nurse is the nurse most needed at the moment, but there is neither the time nor the opportunity to provide postgraduate work in this field. Therefore, the basic curriculum must prepare her for community service as well as hospital service. It is necessary that she be able to teach the control of communicable diseases, maternal and child care, nutrition and sanitation within the understanding and the social and economic structure of the area.

The independent development of nursing education in different regions of the world will be a fascinating process to watch in the coming years. However, if American nurses are to be even aware of these nursing developments in other countries they must develop a broader understanding and increase their skills in communication, especially in the use of other languages.

WHO is prepared to assist countries to develop their health programs at their own speed. The important thing is that the individual country take the initiative and accept responsibility for planning its own program. This takes time, depending on the stability of the government, the presence of local leadership and the acceptance of health practices by the countries. (Pub. Health Nursing, April 1952, K. M. Leahy)

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Unintentional Confounding in Medical Research

When two factors are always associated in a survey or an experiment, it is impossible to decide whether any results produced by them are due to one or the other or both. In such a case the two factors are said to be confounded.

The danger of unintentional confounding is ever present and it would be reasonable to expect that experimenters, either implicitly or explicitly, should have developed technics that avoid some of its pitfalls. And so they have.

Sometimes they have made a deliberate attempt to pair experimental and control subjects so that certain important factors which might affect the outcome of treatment are equally distributed in the two groups, and not associated with the treatment alone. They may use sham operations to distinguish the effects of any operation from those of a specific one; or give saline injections to separate the effects of the drug from those of the vehicle.

One of the most successful methods has been to lead up to a theory by several different paths; it is unlikely that a confounding factor would crop up in a number of separate situations. The argument has an element of hope as well as of reason, but it often works out well. One of the best illustrations is the work of Harvey on the circulation of blood, where he drew on a variety of experimental evidence to support his thesis. Again, the evidence which located the pace-maker of the heart came partly from embryological studies, partly from comparative anatomy and physiology, and partly from electrophysiology. A final example is the array of evidence gathered by J. S. Haldane to show that so-called vagus apnea following hyperventilation is produced by the lowering of the tension of carbon dioxide in the blood rather than by stimulation of the vagus. The great experimenters of medicine have used this method freely and convincingly, but it is only valid if the different experiments used are independent of one another, and not merely ingenious repetitions of the same central, and possibly false, argument. Many theories, supported by arguments running from (a) to (f) or further, have eventually been overthrown because this point was neglected.

The great contribution of the statistician to the solution of unintentional confounding has been to emphasize the importance of random grouping in the experimental method. If the population from whom the subjects of the experiment are drawn contains some individuals with an unknown characteristic that will have an important effect on the outcome of the experiment, then random grouping ensures a fair chance of their equal distribution. These individuals may be a nuisance because they enlarge the error of the experiment, but the important thing is that they should not bias the results; and random grouping gives efficient, though, of course, incomplete, protection against bias. Sometimes a recognizable characteristic of the subjects of the experiment is known to affect the response being measured and is therefore likely to produce partial confounding. This factor may be qualitative; for example, the sex of an animal may affect its gain in weight during a nutritional experiment. The statistical procedure in such a case is to modify random grouping, to give equal numbers of each sex in the various groups; but such grouping is still essential within the limits of this restriction. In other cases the potentially confounded factor may be quantitative; for example, the initial weight of an animal may affect the response in the same experiment. In this case a record is taken of the initial weights, and the analysis of covariance enables a correction to be made to compensate for differences in these weights between the various groups.

An industrious critic can always find elements of confounding in even the most carefully designed experiment. In this respect confounding is like bias; we should attempt to abolish it as far as practicable, and then come to terms with what remains. The success of the bargain will depend largely on background

knowledge of the problem concerned. And success, however welcome, is only provisional: the process of discovering and eliminating confounding factors must continue as long as progress is made. (The Lancet, 1 March 1952, Colin White)

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Experimental Studies on the Circulatory Responses to Intermittent Positive and Alternating Positive-Negative Pressure Respirators

Resuscitators which produce artificial respiration by changing airway pressure fall into 2 general classes: those producing intermittent positive pressure and those producing positive pressure alternating with a period of negative pressure during expiration. Controversy concerns which type of mechanical respirator possesses the physiologic advantage in resuscitation of the non-breathing individual. Thompson, Quimby and Smith have performed experiments demonstrating that alternating positive-negative pressure machines are capable of producing passive circulation through the body. On the other hand, advocates of the use of intermittent positive pressure alone have suggested that pulmonary edema, or other lung damage, might result from a negative pressure phase.

In addition to the high annual incidence of accidents requiring artificial respiration, the possible necessity of treating thousands of nerve gas casualties suffering from respiratory paralysis makes imperative the determination of the most effective methods of artificial respiration.

The purpose of the present studies was to evaluate the intermittent positive and the alternating positive-negative pressure respirators under the conditions in which they are most likely to be used - a combination of respiratory paralysis and circulatory inadequacy.

Summary and Conclusions.

1. Experimental animals with competent circulatory and respiratory systems tolerate either the positive-negative or the intermittent positive type respirators without significant change in blood pressure or cardiac output.

2. In the presence of respiratory failure and/or circulatory embarrassment, the intermittent positive type machines cause a depression in cardiac output and blood pressure which is sometimes fatal. The positive-negative type machines are distinctly superior in such circumstances, since they maintain adequate cardiac output and blood pressure. This latter type of resuscitator owes its desirability to a more favorable effect on venous return to the heart.

3. The objection that a negative pressure phase during expiration will produce pulmonary edema is not supported by experimental findings or theoretical considerations. (Proj. NM 006 014.01.04, Feb. 1952, LCDR S. W. Handford (MSC) USN & LT J. V. Maloney, Jr. (MC) USN, NMFRL, Camp Lejeune, N. C.)

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Dental Civilian Postgraduate Courses Resumed

A limited number of long postgraduate courses in civilian dental schools and universities, to commence in the Fall of 1952, will again be made available to dental officers in the following subjects:

(a) Periodontology
(b) Oral Medicine
(c) Oral Surgery
(d) Prosthodontia
(e) Pathology
(f) Bacteriology

Dental officers (USN) are requested to inform the Chief, Bureau of Medicine and Surgery via official channels if interested in assignment, for one year, to any of the above listed courses. Those dental officers considered eligible will be instructed by BuMed to submit applications for such training in accordance with the provisions of Article 6-82 Manual of the Medical Department.

Dental officers whose applications for long civilian courses were approved in 1950 and subsequently cancelled due to Korean hostilities will be reconsidered on the basis of eligibility for such training at this time. Applications already received by the Bureau need NOT be resubmitted. (Dental Div., BuMed)

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Course in Medical Aspects of Special Weapons and Radioactive Isotopes

The third course for the fiscal year 1952 in Medical Aspects of Special Weapons and Radioactive Isotopes is scheduled to convene at the U. S. Naval Medical School, Bethesda, Maryland, on Monday, 19 May 1952, and continue to 24 May 1952.

The course will present problems likely to be confronted and technics to be employed by medical and dental officers in the field of radioactivity. The subjects will be presented by speakers of outstanding prominence in their specialities; hence, it is assured the presentation will be interesting and informative to all Medical Department officers.

This course is conducted primarily for the benefit of inactive Reserve Medical Department officers; however, a limited number of officers of the Medical Department on active duty may be given "Authorization Orders" (no expense to the government) in accordance with paragraph 3 of BuPers-BuSandA joint letter of 30 November 1951. Inactive Reserve Medical, Dental, Medical Service Corps and Nurse Corps officers residing in the 1st, 3rd, 4th, 5th, 6th, 8th, 9th Naval Districts and Potomac River Naval Command who desire to attend this course should submit their request for 6 days' training duty to the Commandant's office at the earliest practicable date. Meals and a limited number of sleeping quarters will be available. Quarters will be available on a "first come first served" basis.

It is desired to invite inactive Reserve personnel's attention to the fact that acceptance of orders to attend these courses WILL NOT, in any way, increase the possibility of involuntary recall to active duty of the personnel concerned. Therefore, inactive Reserve Medical Department personnel are encouraged to take advantage of this opportunity to attend this course on active training duty orders in a pay status. (Reserve Div., BuMed)

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Physical Examinations for Dependents' Travel

Existing regulations, BuMed Circular Letter 51-80 and U. S. Navy Travel Instructions, paragraph 2000 k (1), require that dependents who desire to travel overseas under Navy auspices obtain prior to departure from home a medical certificate of fitness for travel overseas. This is a prerequisite to the issuance of travel orders from home to the port of embarkation. It is intended to prevent complications and disappointment of those persons who might be turned back at the port of embarkation, as well as to insure the health of the traveler and the protection of his fellow travelers from contagion in the port of embarkation and on board ship.

Medical officers who render dependent care are reminded that pre-travel physical examinations are a requirement of the Navy on all dependents before leaving home for overseas travel. These examinations should be done at the request of the prospective traveler, and should take into account the hazards and rigors of the foreign station, and its medical care facilities, as well as screen out communicable diseases in the applicant. (Preventive Med. Div., BuMed)

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Navy Medical Honorary Civilian Consultants Meet at Navy Department

The Board of Honorary Civilian Consultants to the Medical Department of the Navy met on April 25, 1952, at the Bureau of Medicine and Surgery, Navy Department, Washington, D. C.

The honorary consultants were appointed by the Secretary of the Navy to act as an Advisory Board to the Surgeon General to assist in formulating future policies for the Medical Department of the Navy.

Members of the Board include many of the Nation's outstanding physicians and dentists; the Presidents and Past Presidents of the American Medical and American Dental Associations; Secretary of the American Pharmaceutical Association, and leading educators in the nursing profession. (PIO, BuMed)

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From the Note Book

1. The National Science Foundation has been established as the government agency responsible for a continuing analysis of the whole national endeavor in basic research, including the evaluation of the research programs of other Federal agencies. On the basis of studies now under way, the Foundation will formulate a broad national policy designed to assure that the scope and the quality of basic research in this country are adequate for national security and technological progress. (The President of the United States, Budget Message, 1953)

2. Rear Admiral Lamont Pugh, Surgeon General of the Navy, attended the combined meetings of the Regents and Governors of the American College of Physicians, April 20, 1952, at Cleveland, Ohio. He is a Fellow of the American College of Physicians, and Governor for the Navy in that College. On April 21, Admiral Pugh went to Cincinnati, where he delivered an address on industrial medicine within the Naval establishment before the Fourth Annual Navy Industrial Health Conference which convened April 19 through 24. (PIO, BuMed)

3. In the event of catastrophe resulting from enemy action against a metropolitan area, it is of utmost importance that civil defense activities be as prompt and efficient as possible; that the public be assured that the sick and injured, women and children are receiving adequate attention; that the requirements of emergency workers be met to the extent necessary to get the work done, and that good morale be maintained and panic avoided. In times of crisis, food and feeding are basic morale factors and often determine recovery from disease and injury. (Am. J. Pub. Health, April 1952, R. S. Goodhart & N. Jolliffe)

4. Two books for civilian defense planners are recommended: (1) Civil Defense in Modern War, by Brig. Gen. A. M. Prentiss, USA (Ret.); (2) Air War and Emotional Stress, by Dr. I. L. Janis. Both books are published by McGraw-Hill Book Company, Inc., New York, N. Y.

5. Sixty-nine fires and explosions occurring in hospitals of the United States, with the causes, have been reported. An incidence rate of 8 explosions due to static will occur each year in the United States. (Am. J. Surg., April 1952, B. J. Ciliberti & P. M. Wood)

6. Three important and highly significant papers on the fascinating and tragic problem of retrolental fibroplasia will be found in the March 1952 issue of the American Journal of Ophthalmology.

7. The surgeon of today and tomorrow should be able to make a decent living, but if he is worthy to succeed to the standards of New England surgery, he must labor for eminence in his profession, respect in his community, and work well done for humanity. The surgeon must see, for the benefit of the patient of tomorrow, that the staff of Aesculapius is ever the symbol of progress

and freedom. (New Eng. J. Med., 13 March 1952, W. J. Mixter)

8. A comparison study of pole top and other manual resuscitation methods appears in Industrial Medicine and Surgery, April 1952, by A. S. Gordon, M. S. Sadove, F. Raymon & A. C. Ivy)

9. A team of food sanitation and training experts representing the Armed Forces and the U. S. Public Health Service has undertaken a joint effort toward standardizing and improving instruction in prevention of foodborne disease outbreaks. Twelve cities in key military areas in the United States are being visited in order to indoctrinate teaching personnel of military and civilian health groups in the use of a new PHS Manual, "Instructors' Guide - Sanitary Food Service." The publication, which has been adopted as the official instructors' guide in the Navy, Air Force and U. S. Public Health Service, is available at the Government Printing Office, Washington 25, D. C. ($1.50 per copy). (PIO, BuMed)

10. The radiosensitivity of the embryo and fetus is a matter of great practical importance to radiologists, gynecologists and obstetricians. Whenever possible, irradiation involving the uterus in women of childbearing age should be restricted to the 2 weeks following the last menstrual period, to preclude the possibility of fertilization having taken place; and the present practice of avoiding irradiation during a known pregnancy, particularly during the later stage, should not be relaxed. (Radiology, March 1952, L. B. Russell & W. L. Russell)

11. The modern trends in obstetrics and anesthesia emphasize the need of exercising judgment, skill and mutual confidence of the obstetrical team, composed of the obstetrician, the anesthesiologist and their co-workers, if the lives of mother and baby are to be safeguarded during childbirth. (Am. J. Obstet. & Gynec., March 1952, B. B. Hershenson)

12. It has now been proved that DDS (Diamino-diphenyl sulphone), once supposed to be too toxic for use in man, is no more toxic than its derivatives, and is much simpler and much more economic for use in the treatment of leprosy. (Tr. Roy. Soc. Trop. Med. & Hyg., March 1952, E. Muir)

13. The structure and properties of ice are discussed in Science, 10 April 1952, by N. Bjerrum, Copenhagen.

14. About 100 miles of glass fiber can be spun from a glass marble. (Science News Letter, 12 April 1952)

15. Triethylene glycol vapor, under the conditions of its use in treating the dormitories housing Navy recruits, was ineffectual in the prevention of epidemics of influenza, streptococcal infections and other acute respiratory infections. (Am. J. Hyg., March 1952, Personnel NAMRU # 4, Res. Proj. NM 005 051.05)

16. Naval Medical Corps officers recently certified in their specialties by American Boards are: CDR J. D. Langston (American Board of Pathology); LCDR W. S. Stryker (American Board of Orthopedic Surgery), and LCDR T. D. Yocum (American Board of Orthopedic Surgery). (PIO, BuMed)

17. A simple holder for Wangensteen suction tubes consists of an old metal eyeglass frame with 2 rings attached bilaterally; 1 ring is attached to the lower circumference of the eyeglass rim and the other ring is attached to the horizontal bow which extends to the ear. Two identically placed rings are also attached to the other side of the eyeglass rim. The nasal tube passing out from the nose is sustained by the first ring and then passes outward toward the second ring and backward toward the ear to the suction bottle. In this way, all adhesive tape is eliminated, and the patient rests much more comfortably. (Am. J. Surg., April 1952, F. Ciampa)

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List of Recent Reports Issued by Naval Medical Research Activities

U. S. Naval School of Aviation Medicine, U. S. Naval Air Station, Pensacola, Fla.

The Oculogravic Illusion, NM 001 059.01.27, 29 December 1951.

Medical Research Laboratory, U. S. Naval Submarine Base, New London, Conn.

Theoretical Considerations of the Use of The Air-Filled Submarine Escape Appliance From Great Depths, NM 002 015.08.01, 27 January 1952.

The Decline of Pitch Discrimination With Time, NM 003 041.22.03, 28 January 1952.

U. S. Naval Medical Research Unit # 3, Cairo, Egypt

Studies on Urinary Carriers of Enteric Group Organisms, IV. Urinary Agglutinins in Uninoculated Chronic Urinary Carriers, NM 005 050.07.03, 30 January 1952.

A New Piroplasm From the Rock Hyrax, NM 005 050.39.15, 27 February 1952.

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ALNAV 9 10 April 1952

Subj: Administration of Obligated Funds

AlNav 9. Basegram. Attention all commands receiving allotments, project orders or other authorizations to obligate funds invited to Department of Defense directive of 20 March issued pursuant to Section 3679 Revised Statutes as amended by General Appropriation Act of 1951 which sets forth regulations governing administrative control of appropriations. Regulations and implementing instructions within Navy being distributed by NavComp instruction 7000.2. Purpose is to restrict obligations and expenditures against each appropriation or fund, allocations, allotments, and suballotments thereunder to the amounts of such authorizations and to provide penalties for violations. Essential that provisions of NavComp instruction be brought to attention of all personnel concerned with the administration or obligation of funds.

John F. Floberg

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BUMED CIRCULAR LETTER 52-37 1 April 1952

From: Chief, Bureau of Medicine and Surgery
To: All Ships and Stations having Medical Officer Personnel Aboard

Subj: Non-naval professional examinations and memberships in civilian professional societies for medical officers; information concerning

Ref: (a) BuMed Circular Letter No. 50-62

1. Reference (a) is hereby canceled.

2. In order that the personnel records maintained in the Bureau of Medicine and Surgery concerning medical officers may contain all information required for orderly personnel planning, it is necessary that this Bureau be kept informed of any professional examinations, other than examinations for promotion, in which an officer intends to participate. Specifically, this includes examinations by specialty boards or state or national boards of medical examiners and which require that the candidates be assembled at a given time or place.

3. It is the responsibility of each officer to notify promptly this Bureau concerning impending examinations of this type. This notification should be in the form of an official letter forwarded via official channels to the Chief of the Bureau of Medicine and Surgery, giving exact information regarding the title of the examining body, the nature and purpose of the examination, and the place and date on which it will be given.

4. Medical officers who consider themselves eligible to apply for permission to take the examination for certification by an American Specialty Board are required to apply directly to the Bureau of Medicine and Surgery for an evaluation of their formal training credits.

5. Applicants for admission to membership in the American College of Surgeons or the American College of Physicians are to submit their applications to the Bureau of Medicine and Surgery for evaluation and endorsement by the Surgeon General.

6. It is requested that a certified or photostatic copy of notification of the results of such examination or membership appointment be forwarded to this Bureau for incorporation in official records.

7. Every effort will be made, contingent upon the needs of the service, to retain officers at stations for reasonable periods of time in order that they may participate in the above examinations. The highest priority for retention will be given for specialty board examinations.

H. L. Pugh

The above letter will not be printed in the Navy Department Bulletin.

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BUMED CIRCULAR LETTER 52-38 10 April 1952

From: Chief, Bureau of Medicine and Surgery
To: All Ships and Stations

Subj: Submission of NAVMED-U, (Report of Medical, Dental and Hospital Treatment of the Personnel of the Navy and Marine Corps by other than the Medical Department of the Navy); revised requirements for

Ref: (a) Ch. 20, ManMedDept

1. A NAVMED-U report is now required only when active duty Navy or Marine Corps personnel are rendered civilian or U. S. Public Health Service medical, dental or hospital care, service, or treatment.

2. Appropriate changes in reference (a) are being made.

C. J. Brown
Acting

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BUMED CIRCULAR LETTER 52-39 10 April 1952

From: Chief, Bureau of Medicine and Surgery
To: All Ships and Stations to Which are Attached Hospital Corps Personnel on Duty Independent of a Medical Officer

Subj: Reference book for Hospital Corps personnel on independent duty

Ref: (a) BUMED Cir Ltr No. 50-48
(b) BUMED Cir Ltr No. 52-23; NDB of 15 March 1952

1. Reference (a) is hereby cancelled and superseded. In lieu of the textbooks previously provided under reference (a), the Bureau will now furnish to addressees, on request, a copy of the 1939 edition of the Handbook of the Hospital Corps, United States Navy.

2. As indicated in reference (b), the 1939 Handbook will be issued on a ship-and-station basis only. No personal copies will be supplied.

3. The supply of the 1949 edition of the Handbook has been exhausted. The new edition will be available for distribution late in 1952 at which time copies will be forwarded to addressees without request.

4. This letter shall be considered cancelled when no longer of use to the addressee.

H. L. Pugh

The above letter will not be printed in the Navy Department Bulletin.

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JOINT LETTER

BUMED CIRCULAR LETTER 52-40 10 April 1952

From: Chief, Bureau of Medicine and Surgery
Chief of Naval Personnel
To: U. S. Navy Recruiting Station and Office of Naval Officer Procurement

Subj: Tests Used in the Selection and Classification of Student Naval Aviators and Student Naval Aviation Pilots; Cancellation of Joint Letter Concerning

Ref: (a) Joint BUMED-BUPERS Letter of 15 March 1944; BUMED CIR LTR 44-45; BUPERS 364-WDJ ON/23 Procurement Directive No. 13-44

1. Having served its purpose, reference (a) is hereby cancelled.

2. After the above cancellation action has been noted, this letter shall also be considered cancelled.

H. L. Pugh L. T. Dubose

The above letter will not be printed in the Navy Department Bulletin.

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Change of Address

Please forward requests for change of address for the News Letter to: Commanding Officer, U. S. Navy Medical School, National Naval Medical Center, Bethesda 14, Maryland, giving full name, rank, corps and old and new address.

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